Citation:

Mennella JA, Pepino MY, Teff KL. Acute alcohol consumption disrupts the hormonal milieu of lactating women. J Clin Endocrinol Metab. 2005 Apr;90(4):1979-85. Epub 2004 Dec 28. PMI 15623810

PubMed ID: 15623810

Study Design:

randomized crossover trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The study purpose was to determine whether alcohol consumption disrupts the hormonal response in lactating women. Prolactin and oxytocin, two key hormones involved in lactation, were examined in terms of their response to alchol intake.

Inclusion Criteria:

- nonsmoker
- healthy
- lactating woman exclusively nursing infants ages two to four months
- Subjects gave written informed consent before participating in the study.

Exclusion Criteria:

- lifetime alcohol abstainers
- taking any medications (including oral contaceptives)
- women who had resumed menstruation
- smokers
- lactating women with babies younger than two months or older than four months of age

Description of Study Protocol:

Recruitment

Recruitment was from ads in local newspapers and newsletters.

Design

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- The impact of alcohol on hormone levels was examined. Subjects consumed alcohol in orange juice on one test day and alcohol alone on a different test day.
- within-subjects design
- controlled for time of day
- order of testing was randomized between subjects

Blinding used (if applicable)

- To mask smell and flavor, alcohol (3 ml) was placed on the surface of cups served to subjects.
- Nurses were blinded to conditions.

Intervention (if applicable)

- Subjects arrived at the testing laboratory at the same 0800 h (±30 min) on both days of testing. An iv line was placed in the antecubital vein of the arm and after an acclimatization period, blood samples were collected at set intervals before beverage consumption.
- One of two beverages was served on each of the testing days:
    - Alcohol condition: 0.4 g/kg alcohol in orange juice (15% vol/vol)
    - Control condition: equal volume of orange juice
- Subjects pumped their breast with an electric breast pump (stimulation of alternating breasts) for 16 minutes.
- Blood samples were then taken at set intervals before, during and after breast pump stimulation to measure levels of hormones.
- The amount of milk pumped during the 16-minute stimulation period and the latency to eject the first milk droplet were measured.
- Blood alcohol concentrations were measured.
- Self-reported alcohol efffects were assessed by having subjects complete the Addiction Reserach Center Inventory (ARCI).

Statistical Analysis

- Separate repeated measures mixed ANOVA used to test for significant differences in prolactin, oxytocin, cortisol, blood alcohol concentrations and self-reported drug effects; experimental condition and time were within-subjects factors.
- *post hoc* Fisher least significant difference analysis was used when significant.
- Area under the curve (AUC) values were calculated using a point-to-point method; peak hormone values were compared with baseline values from baseline to the end of the test session.
- Paired t-tests compared peak hormone values and AUC between experimental conditions.
- $P < 0.05$ was considered significant.

Data Collection Summary:

Timing of Measurements

- Testing was performed on two days separated by one week (± 2 days).
- An iv line was placed approximately 30 minutes after subjects arrived at the testing center followed by a 45 minute acclimatization period.
- Blood samples were collected at 40, 25 and 10 minutes before subjects consumed either alcohol in orange juice or orange juice alone.
- Approximately 35 minutes after beverage consumption began, blood samples were collected

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every two minutes for 16 minutes (35, 37, 39, 41, 43, 45, 47, 49 and 51 minutes after beverage) while women pumped their breasts.
- Blood samples were also taken after breast pumping stopped every 15 minutes for 90 minutes (65, 80, 95, 110, 125, and 140 minutes).
- Hormone assays were used to measure oxytocin, cortisol and prolactin in plasma samples.

Dependent Variables

1) Plasma levels of:

- oxytocin (pg/ml)
- prolactin (ng/ml)
- cortisol (µg/ml)

2) Blood alcohol concentrations (g/liter) estimated from breath alcohol measurements.

3) Self-reported drug effects measured by questionnaire:

- sedation
- dysphoria and somatic effects
- drunkedness

4) Milk ejection latency (seconds) - time to eject the first milk droplet

5) Milk production (ml) during 16 minute pumping period

Independent Variables

Two test conditions:

- Alcohol (alchol in orange juice)
- Control (orange juice alone)

Time relative to beverage consumption (minutes)

Control Variables

Description of Actual Data Sample:

Initial N: 17 lactating women (6 primiparous, 11 multiparous)

Attrition (final N): 17. No attrition was reported.

Age: average age: 31.9 ± 1.2 years

Ethnicity:

Caucasian: n = 10

African American: n = 5

Asian: n = 1

Another ethnic group: n = 1

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Other relevant demographics

Women reported low alcohol consumption during pregnancy: mean standard drinks per month = 0.2 ± 0.1. Alcohol consumption was significantly increased during lactation to an average drinks per month = 1.5 ± 0.6.

The authors stated that the above numbers are likely to underestimate alcohol consumption.

Anthropometrics

mean body mass index: 26.4 ± 1.1 kg/m^2

Location:

General Clinical Research Center, University of Pennsylvania

Summary of Results:

Key Findings

- Key hormones involved in lactational performance were disrupted following alcohol consumption:
  - oxytocin levels significantly decreased after alcohol consumption.
  - prolactin levels significantly increased during and after breast stimulation on the day alcohol was consumed.
- Decreased oxytocin response on the alcohol day was significantly related to decreased milk yield and milk ejection latency.
- Changes in prolactin were related to self-reported measures of drunkedness.
- Cortisol levels were increased during the alcohol test session, but were were not significantly correlated with oxytocin, prolactin, milk ejection latency, amount of milk expressed or self-reported measures of drug effects.
- The authors concluded that decreasing levels of cortisol observed on the control day suggested that the experimental procedures were not stressful to the subjects.

Other Findings

<u>Oxytocin:</u>

- Oxytocin levels were significantly decreased during and after breast stimulation during the alcohol condition as compared to the control condition.
- Oxytocin AUCs were on average 78% (±26.6) smaller for alcohol vs. control condition.
- Significant correlations between oxytocin AUC during breast stimulation and milk ejection latency were not observed, but lower levels of oxytocin were correlated with longer ejection latency during the initial minutes of breast stimulation (t = 35-37) on the alcohol day.
- Peak oxytocin levels were not significantly different (alcohol day vs. control day).
- Individual differences between subjects in oxytocin response were preserved - oxytocin AUCs were correlated on the alcohol and the control day
- Less oxytocin was produced by 12 of the 17 women during breast stimulation on the alcohol day as compared to the control day ($p < 0.05$). Lower milk yields were observed for these women that produced 13 ± 7% less milk than the other women during pumping.

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- No significant relationship was observed between self-reported indices of drug effects and oxytocin AUCs/levels on either the control or alcohol day.

Prolactin:

- Prolactin levels were significantly increased with alcohol consumption both during and after breast stimulation.
- During the alcohol session peak prolactin levels were significantly higher and the AUCs significantly increased by 336% (±222) as compared to the control session.
- 76% of women tested displayed this enhanced response. ($p = 0.02$)
- In the control condition, no significant relationships were found between prolactin and amount of milk expressed or milk ejection latency. (all p values > 0.10)
- In the alcohol condition, prolactin AUCs during breast stimulation were significantly correlated with milk ejection latency; higher prolactin levels were correlated with longer ejection latency.
- There was no correlation between prolactin AUCs and oxytocin AUCs during breast stimulation on the control vs. alcohol days.
- Drunkedness ratings were significantly correlated with relative increases in prolactin levels when BAC levels were peaking.

Cortisol:

- Cortisol levels were significantly higher in the alcohol condition as compared to the control condition; peak cortisol was significantly higher when alcohol was consumed, but there was no significant difference between the two conditions in cortisol AUCs.
- Cortisol AUCs were not significantly correlated with oxytocin or prolactin AUCs.
- Cortisol levels or AUCs were not related to indices of lactational performance (milk ejection latency, amount of milk expressed) or self-reported drug effects.
- The authors concluded that decreasing levels of cortisol observed on the control day suggested that the experimental procedures were not stressful to the subjects.

Blood alcohol concentration (BAC):

- Peak BAC was observed 43-51 minutes after alcohol intake and then decreased.
- When women drank alcohol, feelings of sedation, dysphoria and drunkedness significantly increased, paralleling changes in blood alcohol levels.

Author Conclusion:

Key hormones involved in lactation, prolactin and oxytocin, are disrupted by alcohol consumption. Prolactin levels are increased whereas oxytocin levels are decreased during breast stimulation. The results of this study apply to the short-term consequences of alcohol on lactation hormones, but the long term consequences of disruption in these hormones in terms of lactation perfomance remains unknown.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

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1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A

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3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes

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6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes

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	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes

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